MMUT gene

methylmalonyl-CoA mutase

Normal Function

The *MMUT* gene provides instructions for making an enzyme called methylmalonyl CoA mutase. This enzyme is active in mitochondria, which are specialized structures inside cells that serve as energy-producing centers.

Methylmalonyl CoA mutase is responsible for a particular step in the breakdown of several protein building blocks (amino acids), specifically isoleucine, methionine, threonine, and valine. The enzyme also helps break down certain types of fats (lipids) and cholesterol. First, several chemical reactions convert the amino acids, lipids, or cholesterol to a molecule called methylmalonyl CoA. Then, working with a compound called adenosylcobalamin (AdoCbl), which is a form of vitamin B12, methylmalonyl CoA mutase converts methylmalonyl CoA to a compound called succinyl-CoA. Other enzymes break down succinyl-CoA into molecules that are later used for energy.

Health Conditions Related to Genetic Changes

Methylmalonic acidemia

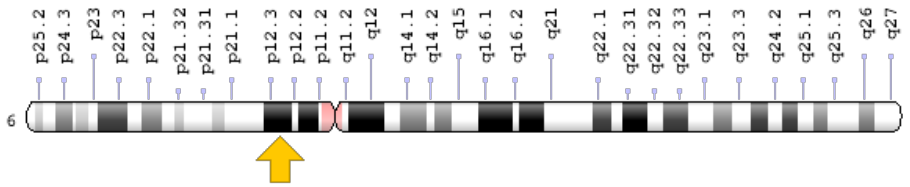
More than 200 mutations in the *MMUT* gene have been identified in people with methylmalonic acidemia, a condition characterized by feeding difficulties, developmental delay, and long-term health problems. These genetic changes prevent the production of functional methylmalonyl CoA mutase or reduce the activity of the enzyme. As a result, certain proteins and lipids are not broken down properly. This defect allows methylmalonyl CoA and other toxic compounds to build up in the body's organs and tissues, causing the signs and symptoms of methylmalonic acidemia.

Mutations that prevent the production of any functional methylmalonyl CoA mutase lead to a form of methylmalonic acidemia designated mut^0. Mut^0 is the most severe form of this disorder and has the poorest outcome. Mutations that alter the structure of the enzyme but do not completely eliminate its activity lead to a form of the condition designated mut^-. The mut^- form is typically less severe, with more variable symptoms than the mut^0 form.

Chromosomal Location

Cytogenetic Location: 6p12.3, which is the short (p) arm of chromosome 6 at position 12.3

Molecular Location: base pairs 49,430,360 to 49,463,298 on chromosome 6 (Homo sapiens Updated Annotation Release 109.20200522, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- MCM
- methylalonyl-CoA mutase
- methylamlony-CoA isomerase
- methylmalonyl CoA mutase
- methylmalonyl Coenzyme A mutase
- methylmalonyl Coenzyme A mutase precursor
- MUT
- MUTA_HUMAN

Additional Information & Resources

Educational Resources

- Basic Neurochemistry (sixth edition, 1999): Methylmalonyl-CoA mutase deficiency prevents the isomerization of methylmalonyl-CoA to succinyl-CoA https://www.ncbi.nlm.nih.gov/books/NBK27933/#A3117
- Biochemistry (fifth edition, 2002): Propionyl CoA Is Converted into Succinyl CoA in a Reaction That Requires Vitamin B12 https://www.ncbi.nlm.nih.gov/books/NBK22387/#A3065

Clinical Information from GeneReviews

- Isolated Methylmalonic Acidemia https://www.ncbi.nlm.nih.gov/books/NBK1231

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28MUT%5BTI%5D%29+OR+%28methylmalonyl+Coenzyme+A+mutase%5BTIAB%5D%29+OR+%28methylmalonyl+CoA+mutase%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- METHYLMALONYL-CoA MUTASE
  http://omim.org/entry/609058

Research Resources

- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=MMUT%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:7526
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:4594
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/4594
- UniProt
  https://www.uniprot.org/uniprot/P22033

Sources for This Summary

- Acquaviva C, Benoist JF, Pereira S, Callebaut I, Koskas T, Porquet D, Elion J. Molecular basis of methylmalonyl-CoA mutase apoenzyme defect in 40 European patients affected by mut(o) and mut- forms of methylmalonic acidemia: identification of 29 novel mutations in the MUT gene. Hum Mutat. 2005 Feb;25(2):167-76.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15643616
- Benoist JF, Acquaviva C, Callebaut I, Guffon N, Ogier de Baulny H, Mornon JP, Porquet D, Elion J. Molecular and structural analysis of two novel mutations in a patient with mut(-) methylmalonyl-CoA deficiency. Mol Genet Metab. 2001 Feb;72(2):181-4.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11161845
- Chandler RJ, Venditti CP. Genetic and genomic systems to study methylmalonic acidemia. Mol Genet Metab. 2005 Sep-Oct;86(1-2):34-43. Epub 2005 Sep 22. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16182581
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2657357/
- Fuchshuber A, Mucha B, Baumgartner ER, Vollmer M, Hildebrandt F. mut0 methylmalonic acidemia: eleven novel mutations of the methylmalonyl CoA mutase including a deletion-insertion mutation. Hum Mutat. 2000 Aug;16(2):179.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10923046

- Hörster F, Baumgartner MR, Viardot C, Suormala T, Burgard P, Fowler B, Hoffmann GF, Garbade SF, Kölker S, Baumgartner ER. Long-term outcome in methylmalonic acidurias is influenced by the underlying defect (mut0, mut-, cblA, cblB). Pediatr Res. 2007 Aug;62(2):225-30.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17597648
- Manoli I, Sloan JL, Venditti CP. Isolated Methylmalonic Acidemia. 2005 Aug 16 [updated 2016 Dec 1]. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, Bird TD, Ledbetter N, Mefford HC, Smith RJH, Stephens K, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from http://www.ncbi.nlm.nih.gov/books/NBK1231/
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301409
- Peters HL, Nefedov M, Lee LW, Abdenur JE, Chamoles NA, Kahler SG, Ioannou PA. Molecular studies in mutase-deficient (MUT) methylmalonic aciduria: identification of five novel mutations. Hum Mutat. 2002 Nov;20(5):406.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12402345
- Worgan LC, Niles K, Tirone JC, Hofmann A, Verner A, Sammak A, Kucic T, Lepage P, Rosenblatt DS. Spectrum of mutations in mut methylmalonic acidemia and identification of a common Hispanic mutation and haplotype. Hum Mutat. 2006 Jan;27(1):31-43.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16281286

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/MMUT

Reviewed: July 2011
Published: June 23, 2020

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services